UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,981	10/29/2001	Eberhard Hildt	033392-001	7240

2387 7590 03/10/2005

OLSON & HIERL, LTD.
20 NORTH WACKER DRIVE
36TH FLOOR
CHICAGO, IL 60606

EXAMINER	
HILL, MYRON G	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 03/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/830,981	HILDT ET AL.	
	Examiner	Art Unit	
	Myron G. Hill	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3)☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 1117204

4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

5)☐ Notice of Informal Patent Application (PTO-152)

6)☐ Other: _____.

DETAILED ACTION

This action is in response to paper filed 22 November 2004.

Claims 21-38 are under consideration in this action.

Information Disclosure Statement

A signed copy of the IDS paper filed 11/22/2004 is enclosed.

Objections Withdrawn

Drawings

The drawings were objected to under 37 CFR 1.83(a) because Figures 3- 5 contain unclear graph lines which will not reproduce well. Additionally, the captions referred to color and sequences.

Applicant has submitted replacement figures that have clear lines, do not refer to colors, and identify the SEQ ID#s.

Claim 2 was objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Applicant has canceled the claim.

Rejections Withdrawn

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 2 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant has canceled the claims.

Claims 1 and 2 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims have been canceled.

Claim Rejections - 35 USC § 102

Claims 1 and 2 were rejected under 35 U.S.C. 102(b) as being anticipated by Wiepreht.

The claims have been canceled.

New Rejections

New Matter

Claim Rejections - 35 USC § 112

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 21-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant has amended the claims to recite "hydropathy values" in place "hydrophobic" and "hydrophilic" as well as requiring the values to be of the "side chains".

Support for this amendment is not seen by the examiner and Applicant is requested to specifically point it out.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is not clear what amino acids are required by

formula in claim 21. There appears to be disagreement between textbooks and page 3 of the specification when using limitation in the claim as written.

For example, it is noted that tryptophan is allowed on page 3 in position 2 as hydrophobic but is not allowed by claim 21 which requires a positive hydropathy value (tryptophan has a negative hydropathy value, Lehninger, page 113).

Claim Rejections - 35 USC § 112

Claims 21-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for all peptides that are contained in the genus of peptides that have the motif of claim 21 or fusion proteins that comprise the motif. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate with these claims.

Instant claims are evaluated for enablement based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows:

(1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The claims are drawn to a 12-mer motif that enables a peptide to be cell permeable (claim 21). The claims are also drawn to fusion peptides comprising the 12-mer motif that include hormones, structural proteins plasma proteins etc. The claims dependent claims include any polypeptide that comprises the 12-mer motif.

The prior art does not teach 12-mer peptides that have the recited hydrophobic/hydrophilic formula that are a genus of discrete peptides that have the recited function. Structures associated with membrane permeability properties have been noted, see Wiepreht (abstract and first page, from IDS). As taught in Wiepreht, even though a core structure was used, each substitution had to be tested to determine the change to the property of the peptide. Even knowing a structure/formula for a motif that leads to permeability, Wiepreht had to test each mutation to determine any change in permeability.

Applicant only provides examples of HBV peptides from the same protein that have similar hydrophobic/hydrophilic assignments in the region of interest (see Figures 3- 5).

The only working example shows in Example 4 DHBV 12-mer peptide linked to GFP functions in vitro. The other example, Example 1, does not show that the bioactivity is specific for the CPP because the control tests a different protein so it cannot be ruled out the PLAP has the same function as a CPP.

Both claim 21 and 30 read on more than just this one sequence.

There are no examples of a synthetic peptide (not derived from HBV) that have the claimed property or the showing of the motif in other known proteins where the

function can be correlated to the same property. There is not a showing that the motif confers the claimed property. Furthermore, the ambiguity of where to assign residues that fall into different groups, makes it impossible to know what structure the formula requires to have the claimed function or how to interpret a sequence and determine that it does fall within the claimed formula. This will lead to extensive experimentation because many peptides can be interpreted as both comprising the formula and not comprising the formula.

Applicant has not shown that the 12-mer peptide by itself is able to function as claimed.

There are no examples of the range of other polypeptides encompassed by the claims (any fusion protein, structural peptides, interferons, cytokines, TNF, plasma proteins, etc.). Applicant has not shown that linking the 12-mer to any other polypeptide will be able to be transported into the cell. The other polypeptides are large and small and have complex structures and it is not known that they can be taken up by the cell when attached to the CPP.

The scope of example provided is not commensurate with the claims which read on the large number possible 12-mer peptides that fit the motif and the large range of fusion proteins claimed.

Applicant has shown one example (# 4) of fusion protein but this example is not commensurate in scope with the claims because GFP is well known as a marker and is known to be stable in cells. The claims are drawn to any fusion protein comprising the motif and it is not known if any protein can be carried across the membrane.

Furthermore, many proteins, especially larger proteins, have complex structures would not have termini that are exposed when the 12-mer is linked to it and thus will not be transported across the cell membrane.

There is no evidence that this motif works on all cell types and in vivo.

Thus, it would require undue experimentation to determine the possible peptides that function as claimed by the motif and determine if all the possible fusion proteins work to make and use the invention as now claimed.

Claim Rejections - 35 USC § 112

Claims 21-29 and 31-38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant disclosure, the applicants have only disclosed the sequence identified as SEQ ID NO: 4 (DHBV) which is directed to the cell permeability peptide (CPP) linked to a second polypeptide (Example 4). No other sequences which "comprise, comprises, or comprising" SEQ ID NO: 4 were disclosed. The specification does not set forth the metes and bounds that encompass the motif of claim 21, there is not enough information about it in literature either to guide the one of skill in the art to predict the undisclosed peptides will function as claimed. Therefore, a written description of the other claimed sequences encompassed by the motif are required. Also, a written

description of the other claimed sequences of fusion proteins that comprise SEQ ID NO: 4 should be disclosed to overcome this rejection. See also *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism. The instant application fits the pattern of *University of California v. Eli Lilly and Co.* for the following reasons:

Applicant shows one peptide from HBV and states that it contains a motif and that the motif can be used to determine any member of the genus of other peptides with the same function. Applicant describes one fusion protein (Example 4) but claims any protein that comprises that sequence.

35 USC 112 requires *inter alia* that a patent specification contain a written description of the invention and the manner and process of making and using it "in such full clear and concise terms as to enable one skilled in the art ... to make and use" the invention. Case law has made it clear that the requirements for a "written description" and an "enabling disclosure" are separate. For example, where a specification contains sufficient information to enable a skilled chemist to produce a particular compound because it gives detailed information on how to produce analogous compounds but it makes no reference to the compound in question, the "written description" requirement has not been met even though the description may be enabling.

With the exception of the fusion polypeptide in Example 4 comprising the fragment DHBV surface protein, the skilled artisan cannot envision the encompassed peptides that are not HBV derived or all possible polypeptides that can be linked to it.

Therefore, the claims do not meet the written description provision of 35 USC 112, first paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 22, 23, 27, 31, 32, and 36 are rejected under 35 U.S.C. 102(b) as anticipated by Hildt *et al.* (1995 Oncogene, from IDS).

The claims are drawn to a fusion protein comprising a virus coat fragment and a cell permeability peptide that has the formula as recited in claim 21 or is defined by the sequence ID#s recited in claim 30. The claims are treated as product by process and require only a polypeptide that comprises the sequence of the motif or SEQ ID# because once the polypeptide is made, it reads on any peptide that contains the sequence.

Hildt *et al.* teach that the region of preS/S that is important for dimerization is the region of residues 41-52 (page 2063, column 1, third full paragraph, the same sequence

as SEQ ID# 2 of the application and same motif of the formula of claim 21). This region is expressed as a larger polypeptide of a structural protein (Figure 4).

Thus, Hildt *et al.* anticipate the claimed invention.

Claims 21-23, and 27 is rejected under 35 U.S.C. 102(b) as being anticipated by Van Nieuwstadt *et al.* (WO 98/50426).

Claim 21 is drawn to a 12-mer peptide with residues as defined in the claim.

The hydropathy values used are those of hydrophobic and hydrophilic (positions 2, 5, and 9 are any of A, M, C, F, L, V, or I and positions 3, 4, 8, and 11 are any but A, M, C, F, L, V, or I, the remaining positions can be any residue).

Nieuwstadt *et al.* disclose a peptide SIQTAFNQGAGT (page 31, line 10) and that this peptide is contained in a viral structural protein (Figure 8).

Thus, Nieuwstadt *et al.* anticipate the claimed invention.

Claim 21 is rejected under 35 U.S.C. 102(b) as being anticipated by Evotec Biosystems (DE 19808258).

Claim 21 is drawn to a 12 mer peptide with residues as defined in the claim.

The hydropathy values used are those of hydrophobic and hydrophilic (positions 2, 5, and 9 are any of A, M, C, F, L, V, or I and positions 3, 4, 8, and 11 are any but A, M, C, F, L, V, or I, the remaining positions can be any residue).

Evotec Biosystems disclose a peptide RVSNLAFTVNQT (page 5, line 13).

Thus, Evotec Biosystems anticipate the claimed invention.

Claims 21-23, 27, 30-32, and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by NCBI Accession # 540642 (protein).

Claim 21 is drawn to a 12-mer peptide with residues as defined in the claim.

The hydropathy values used are those of hydrophobic and hydrophilic (positions 2, 5, and 9 are any of A, M, C, F, L, V, or I and positions 3, 4, 8, and 11 are any but A, M, C, F, L, V, or I, the remaining positions can be any residue).

NCBI Accession # 540642 comprises SEQ ID# 2.

Thus, NCBI Accession # 540642 anticipates fusion proteins that comprise SEQ ID#2 that are from virus coat (structural).

Claims 21-23, 27, 30-32, and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by NCBI Accession # 138800 (protein).

Claim 21 is drawn to a 12-mer peptide with residues as defined in the claim.

The hydropathy values used are those of hydrophobic and hydrophilic (positions 2, 5, and 9 are any of A, M, C, F, L, V, or I and positions 3, 4, 8, and 11 are any but A, M, C, F, L, V, or I, the remaining positions can be any residue).

NCBI Accession # 138800 comprises SEQ ID# 4.

Thus, NCBI Accession # 138800 anticipates fusion proteins that comprise SEQ ID#4 that are from virus coat (structural).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 21 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hildt *et al.* (1995 Oncogene, from IDS).

The claims are drawn to a cell permeability peptide that has the formula as recited in claim 21 and is 12 aa long or is defined by the sequence ID#s recited in claim 30.

Hildt *et al.* teach that the region of preS/S that is important for dimerization is the region of residues 41-52 (page 2063, column 1, third full paragraph, the same sequence as SEQ ID# 2 of the application).

While Hildt *et al.* do not make an isolated 12-mer peptide of the sequence of claims 21 and 30, the text clearly points out the 12-mer region and one of ordinary skill in the art at the time of invention would envision a peptide fragment that consists of 12 residues of the sequence taken from pre-S/S (41-52). One of ordinary skill in the art would be motivated to use the 12-mer peptide because it has been shown to facilitate dimerization and transcriptional activation.

Thus, it would be *prima facie* obvious to make the 12-mer peptide of claims 21 and 30 with the expectation of success because Hildt *et al.* point to a 12-mer region that has a specific function.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Myron G. Hill whose telephone number is 571-272-0901. The examiner can normally be reached on 9am-6pm Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Myron G. Hill
Patent Examiner
~~November 12, 2003~~
3/7/05

ALI R. SALIMI
PRIMARY EXAMINER